radical toward decomposition into CO and R$^\bullet$, and strength of the Fe–COR bond, even if these steps occur concertedly. CO insertion does not occur in the case of phenyl and is slower in the case of methyl as compared to the other primary alkyls because the Fe(III)–C bond is stronger in the first two cases than in the others. The facile decomposition of the $^\bullet$COR radical into CO and R$^\bullet$ prevents CO insertion in the Fe(III)–C bond in the case of benzyl and *tert*-butyl. The acyl radical has an electrophilic character that is less pronounced in the case of methyl than the other alkyls, resulting in a poorer insertion to decomposition ratio in the former case than in the latter. The electrophilic character of the $^\bullet$COR radical is also presumably involved in the insertion of CO in the Fe(II)–C bond in the case of *tert*-butyl (combination of $^\bullet$COR with Fe(I)$^-$) in spite of the tendency of the $^\bullet$CO-*t*-Bu radical to decompose into CO and *t*-Bu$^\bullet$.

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Proton Abstraction from Dimethyl(2-substituted-9-fluorenyl)sulfonium Ions. Evidence for Changes in Transition-State Structure[1]

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Abstract: Rate and equilibrium constants for C(9)-^{1}H, -^{2}H, and -^{3}H abstraction from dimethyl(2-substituted-9-fluorenyl)sulfonium tetrafluoroborates (**1a**, X = H; **1b**, X = Br; **1c**, X = NO_2) catalyzed by oxygen and amine bases have been determined by ^{1}H NMR and detritiation in 95% L_2O–5% Me_2SO (v:v) at 28 °C and ionic strength 1.0 M (KCl). The pK_a values are **1a**, 13.7, **1b**, 12.4, and **1c**, 10.6. Rate constants at $\Delta pK = 0$ are $\sim 10^4$ M^{-1} s^{-1}. The modest intrinsic barrier for proton abstraction from **1** is similar to that for the corresponding cyano-activated fluorenes and is attributed to resonance delocalization into the fluorene ring, with little contribution from solvent reorganization. The primary kinetic isotope effects decrease with increasing ΔpK, but do not approach unity even for $\Delta pK > 15$. The secondary solvent isotope effect of $k_{H_2O}/k_{D_2O} = 2.3$ for ^{3}H transfer from **1a** to water and the absence of strong inhibition of ^{1}H and ^{3}H exchange by D_3O^+ show that proton transfer to water is direct. The secondary solvent lyoxide isotope effects of $k_{OD}/k_{OH} = 2.0$ for ^{3}H exchange of **1a** and **1b** are close to the limiting isotope effect of $K_{OD}/K_{OH} = 2.4$ at equilibrium. Brønsted α values for proton exchange from **1a**–**c** decrease with increasing pK_a^{BH} from 0.97 to 0.59 for a series of oxygen anion catalysts and from 0.67 to 0.46 for amine catalysts that span a reactivity range of $>10^5$. The Brønsted β values for catalysis by substituted acetate ions decrease with decreasing pK_a^{CH} from 0.98 to 0.75 and 0.75 to 0.70 for catalysis by amines. These changes are described by the interaction coefficient $p_{xy} = \partial\beta/\partial pK_a^{CH} = \partial\alpha/-\partial pK_a^{BH} = 0.04$–$0.08$. It is concluded that these changes represent changes in transition-state structure that are related to the large intrinsic reactivity of these carbon acids.

We are concerned here with changes in transition-state structure that are manifested by changes in the slopes of structure–reeactivity relationships for proton-transfer reactions.[2-5] Changes in slope that produce curvature in a Brønsted plot have been demonstrated for several proton transfers to and from carbon, including the ionization of acetylacetone[6] and the protonation of diazoacetate anions.[7] There is also precedent for changes in Brønsted slopes with a common set of catalysts for enolization of a series of ketones, keto esters, and diketones,[2,8] for ionization of (4-nitroaryl)-acetonitriles,[9] and for protonation of vinyl ethers.[10] Changes in Brønsted slopes represent second derivatives of log *k* with respect to basicity and can be described by the direct interaction coefficient p_y (eq 1) for curvature in a Brønsted slope, or by the cross-interaction coefficient p_{xy} (eq 2), for changes in Brønsted slopes

$$p_y = \partial\beta/-\partial pK_a^{BH} \qquad (1)$$

$$p_{xy} = \partial\beta/\partial pK_a^{CH} = \partial\alpha/-\partial pK_a^{BH} \qquad (2)$$

when the structures of both the carbon acid and the base catalyst are changed.[3] The available data for proton transfer to and from carbon indicate that the interaction coefficients are generally small, which corresponds to large curvatures of the energy surface at the saddle point for the reaction.[4]

The existence of changes in transition-state structure for proton abstraction from carbon has been questioned, however.[11-16] Several workers, notably Kemp[11] and Bordwell,[12,13] have commented on the lack of evidence for curvature in many Brønsted plots. Even when curvature is observed, it may be caused by changes in the rate-limiting step,[14,16,17] in solvation,[18,19] or in the

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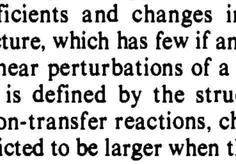
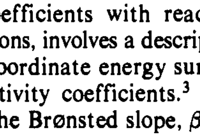
chemical structure of a series of bases.[11,13,20] Furthermore, the interpretation of cross coefficients may be questioned because of the large variations in structure that are necessary to establish changes in the Brønsted slopes for a series of substrates, as in the monoketones and diketones studied by Bell and Lidwell,[8] the large steric effect of the *o*-nitro group in 2,4-dinitrophenylacetonitrile,[9] and the different positions of substituents in vinyl ethers.[10] Kemp has pointed out the importance of these cross-coefficients and noted that the demonstration of such changes "can only be carried out unambiguously with a class of substrates which preserve geometry and gross electronic structure" over a wide range of reactivity and that do not react at diffusion-controlled rates.[11] The reaction of 1-aryl-1-nitroethanes with amines appears to be the only system to meet these criteria rigorously. These reactions show no evidence for a change in the Brønsted β value over a 1000-fold change in reactivity.[12]

An empirical approach to characterizing structure–reactivity coefficients and changes in these coefficients with reactant structure, which has few if any assumptions, involves a description of linear perturbations of a reaction-coordinate energy surface that is defined by the structure–reactivity coefficients.[3] For proton-transfer reactions, changes in the Brønsted slope, β, are predicted to be larger when the carbon acid is changed than when the base catalyst is changed.[3,4] This is because changes in the position of the saddle point parallel and perpendicular to the reaction coordinate tend to cancel for the coordinate defined by β when the base catalyst is changed, so that the change in the effective charge on the catalyst in the transition-state and the direct Hammond effect, as measured by p_y, are small. However, the parallel and perpendicular effects are additive for the cross coefficient p_{xy}, so that a change in the base catalyst is likely to cause a significant change in the "effective charge" on the carbon acid in the transition state.[3] Furthermore, it is easier to measure and to evaluate changes in α and β across a series of reactants when the structure of the second reactant is changed.[11] If the Brønsted coefficients are a function of bond orders in the transition state, this approach describes changes in transition-state structure with changing structure of the reactants.

We describe here an investigation of the rates of proton removal by oxygen and nitrogen bases from dimethyl(2-substituted-9-fluorenyl)sulfonium tetrafluoroborates (**1**) to give the sulfonium ylides **1**$^{\pm}$. These carbon acids are expected to react with a low intrinsic barrier, which should correspond to a small curvature of the energy surface at the transition state and result in relatively large changes in the Brønsted coefficients.[3] Sulfonium ions represent a simple class of carbon acids that are expected to undergo proton loss with minimal changes in structure and solvation of charge; these changes are believed to be largely responsible for the large intrinsic barriers to the ionization of many carbon acids.[2,21,22] These substrates are also of interest because fluorenyl derivatives presumably undergo relatively little change in solvation upon ionization, so that the barrier for proton transfer should largely reflect any requirement for resonance delocalization of the negative charge on carbon.



1a: X = H
b: X = Br
c: X = NO2



1$^{\pm}$

The results show that these ylides are formed with a modest intrinsic barrier and indicate that the barrier for ionization of sulfonium-activated carbon acids is similar to that for the ionization of cyanocarbon acids. The changes in the Brønsted β coefficient with changes in the pK_a of the carbon acid can be described by a cross-coefficient of $p_{xy} = \partial\beta/\partial pK_a^{CH} = 0.04$–$0.08$ for uncharged and anionic bases. The results are consistent with the conclusion that changes in transition-state structure do occur and that the magnitude of these changes is proportional to the intrinsic reactivity of a given carbon acid. This relationship can explain the difficulty in detecting such changes with most carbon acids.

Experimental Section

Materials. All chemicals were reagent grade and were used without further purification unless otherwise stated. Water and 1,1,1,3,3,3-hexafluoro-2-propanol were distilled. Amine hydrochlorides were recrystallized and, except for 2-chloroethylamine hydrochloride, were exchanged in D_2O. Amine deuterochlorides were obtained as lyophilized powders. Organic salts were dried in vacuo at >70 °C overnight. Deuterium chloride, deuterium oxide (>99.8 atom % D), dimethyl-d_6 sulfoxide, and acetic acid-d_1 were obtained from Aldrich and were >98 atom % D. Aquasol-2 scintillation cocktail and $[^3H]H_2O$ (1 Ci/mL) were from New England Nuclear.

Dimethyl-9-fluorenylsulfonium tetrafluoroborate salts were synthesized from the corresponding 2-substituted-9-bromofluorenes (Aldrich) by a modification[23] of the procedure of Ingold and Jessop[24] as described here for **dimethyl-9-fluorenylsulfonium tetrafluoroborate (1a).** To 2.6 g (10.4 mmol) of 9-bromofluorene in 50 mL of nitromethane were added 0.75 mL (10 mmol) of dimethyl sulfide and 2.1 g (10.4 mmol) of silver tetrafluoroborate. The reaction mixture was shielded from light and stirred overnight under argon. The product was separated from AgBr by filtration through 5 cm of Florisil (100–200 mesh) in a sintered glass funnel and washed with chloroform. The combined filtrates were evaporated under vacuum. The crystals were washed several times with cold ether and recrystallized from 1:1 ethanol–acetone: mp 180–182 °C dec; ^1H NMR (300 MHz, 95% D_2O–5% Me_2SO-d_6 (v:v), ref DSS) δ 7.97 (d, 2 H), 7.8 (d, 2 H), 7.65 (t, 2 H), 7.55 (t, 2 H), 5.91 (s, 1 H C(9)-H), 2.54 (s, 6 H, S^+–CH_3); ^{13}C NMR δ 145.0, 134.6, 131.9, 129.5, 124.6, 33.8, 24.1 ppm. **Dimethyl(2-bromo-9-fluorenyl)sulfonium tetrafluoroborate (1b)**: mp 170–180 °C dec; ^1H NMR δ 7.98–7.57 (m, 7 H, Ar), 5.93 (s, 1 H, C(9)-H), 2.62 (s, 3 H, S^+-CH_3), 2.51 (s, 3 H, S^+-CH_3). **Dimethyl(2-nitro-9-fluorenyl)sulfonium tetrafluoroborate (1c)**: mp 220–222 °C dec; ^1H NMR (25% CD_3CN–75% D_2O) δ 8.60 (s, 1 H, C(1)-H), 8.49 (d, 1 H), 8.06 (m, 2 H), 7.70 (m, 3 H), 6.08 (s, <1 H, C(9)-H), 2.68 (s, 3 H, S^+-CH_3), 2.57 (s, 3 H, S^+-CH_3). Dimethyl-[9-^2H]-9-fluorenylsulfonium fluoroborate was obtained from the corresponding protium substrate by stirring overnight in 25% CH_3CN–75% D_2O (v:v) buffered with 10 mM potassium bicarbonate at pD 7. After acidification to pD <2, the solvent was removed under reduced pressure and the crystals were washed twice with cold ether. The product was 95% deuterated at C-9 as determined by ^1H NMR. Dimethyl-2-substituted-[9-^3H]-9-fluorenylsulfonium fluoroborates were obtained in a similar fashion in 50% CH_3CN–50% D_2O (v:v) with tritiated water (0.1 Ci/mL). The $[^3H]H_2O$ was removed by bulb-to-bulb distillaton.

Because the ^1H chemical shift of dichloroacetate overlaps with the C(9) proton of **1a–c**, $Cl_2CHCOO^-K^+$ was exchanged in 0.02 M KOD in D_2O at 40 °C overnight. The solvent was removed under reduced pressure and the residue was neutralized on ice to pH <1 with 7 M DCl. The acid was taken up in ether and dried over Na_2SO_4, and the solvent was evaporated. The acid was neutralized on ice to pH 3.9 with 4 M KOD. The solvent was removed under reduced pressure and the potassium salt was dried under vacuum.

Methods. All reactions were carried out in 95% L_2O–5% Me_2SO (v:v) (L = H or D) at 28 °C and ionic strength 1.0 M, maintained with potassium chloride. Solution pL was measured with an Orion Model 701A pH meter and a Radiometer GK 2321C combination electrode standardized in water. Measurements of the pH at known concentrations of hydroxide ion in 95% H_2O–5% Me_2SO (v:v) at 1 M ionic strength, maintained with potassium chloride, were found to follow eq 3, which was

$$[OL^-] = 0.87 \times 10^{(pL - pK_w)} \qquad (3)$$

used to determine the concentration of lyoxide ion at any value of pL. The autoprotolysis constant of water, $K_w = 1.05 \times 10^{-14}$, in 95% H_2O–5% Me_2SO (v:v) at 28 °C was interpolated from the compilations of Fiordiponti et al.[25] The solvent isotope effect on K_w, $K_w^H/K_w^D = 7.25$, was assumed to be the same as for pure water,[26] and the pD of deuterium

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oxide solutions was obtained by adding 0.4 to the observed pH meter reading.[27] The isotopic composition of the deuterium oxide solutions was always >97% deuterium after addition of all reagents.

C(9) Proton Exchange in D_2O. Rate constants for C(9)-proton exchange in 95% D_2O–5% Me_2SO-d_6 (v:v) at 28 ± 1 °C were determined by FT ^1H NMR on a Varian XL-300 NMR spectrometer. The probe temperature was measured by two methods that agreed to within ±1 °C. First, a thermocouple in the probe was calibrated with use of the chemical shift difference of the methylene and hydroxyl protons of ethylene glycol (containing 0.03% (v:v) concentrated HCl).[28] Second, a sample of dimethyl(2-bromo-9-fluorenyl)sulfonium tetrafluoroborate in 0.01 M DCl was placed in the probe for 15 h and the initial rate of C(9)–^1H exchange ($t_{1/2}$ = 11 h) was determined by ^1H NMR as described below. Similar samples were placed in a water bath at 25.0, 30.1, and 34.9 °C (±0.2 °C) and removed every few hours for integration of the area of the C(9) proton as described below. The temperature of the sample inside the probe was interpolated from an Arrhenius plot of this data.

Samples were vortexed vigorously, and some samples were sonicated to speed dissolution of the substrate, before insertion into 5-mm NMR tubes. Integral ratios, R, of the area of the C(9) proton (δ = 5.9–6.1 ppm) to the area of the aryl C(1–8) or C(1,8) protons (as nonexchanging internal standard) were determined as a function of time. Typically, 5–64 transients (3-s acquisition time) were collected for each time point. For exchange reactions with $t_{1/2}$ >60 min, samples were removed from a water bath at 28 ± 0.2 °C and integral ratios were measured as described above. The pseudo-first-order rate constants were obtained from the slopes of semilogarithmic plots of R against time for 2–3 half-lives. The C(9) proton was completely exchanged and the sulfonium methyl group protons remained unexchanged.

C(9) Deuteron Exchange in H_2O. Pseudo-first-order rate constants for ^2H exchange of dimethyl-[9-^{2}H]-9-fluorenylsulfonium tetrafluoroborate (95% labeled at C(9)) were determined in 95% H_2O–5% Me_2SO (v:v) at 28 ± 0.2 °C. Aliquots (1.5 mL) were quenched with 20 μL of 7 M DCl at various time intervals and immediately frozen in a dry ice–acetone bath. The solvent was removed under reduced pressure with a Savant Speed Vac concentrator and the residues were stored at −10 °C. The residues were then dissolved in 95% D_2O–5% Me_2SO-d_6 (v:v) containing 0.1 M DCl and integral ratios, R, were determined as described above. Semilogarithmic plots of $R_\infty - R_t$ against time were linear over 3 half-lives and extrapolated to $R_\infty - R_t = 0.95$ at zero time; this showed that no significant exchange occurred during concentration or analysis of the samples.

C(9) Triton Exchange in H_2O and D_2O. Pseudo-first-order rate constants for C(9)-triton exchange were determined at 28 ± 0.2 °C by measuring the nonvolatile radioactivity remaining from C(9)-tritiated substrates **1a** and **1b**. Typically, 10 μL of a 0.1–1 mM solution of substrate (~0.5 μCi/μmol) was quenched with 10 μL of 1 M HCl for **1a**, or 3 M HCl for **1b**, in the flat-bottomed wells of a polystyrene microtiter plate (Becton-Dickenson). The quenched samples were absorbed onto Whatman 3 MM filter paper (5 × 20 mm). Volatile tritiated water was removed by air-drying overnight for **1a**. The half-life for exchange from **1b** in 3 M HCl is ~30 h, so that the polystyrene plate containing the quenched samples was kept on dry ice during the assay in order to avoid the possibility of ^3H exchange from **1b** on the quenched filter paper. Periodically between time points, the plate was placed in a vacuum desiccator and tritiated water was evaporated rapidly under vacuum from a water aspirator. Control experiments showed that >90% of [^{3}H]H_2O was removed from the filter paper in 30 min by this method. The dried filters were placed in scintillation vials containing 1 mL of water and 15 mL of scintillation cocktail and shaken intermittently over several hours until no schlieren were observed. Samples were counted for ≥10 min with a Beckman LS-6800 scintillation counter. Endpoints were obtained after $>10t_{1/2}$ and were typically 25–75 cpm. The pseudo-first-order rate constants were obtained from the slopes of semilogarithmic plots of cpm$_t$ − cpm$_\infty$ against time for 10 time points. Some samples of dimethyl-[9-^{3}H]-9-fluorenylsulfonium tetrafluoroborate had 200–500 cpm at t_∞ compared with 25–50 cpm for control samples containing only [^{3}H]H_2O; this presumably represents unexchanged tritium in the sulfonium methyl groups.

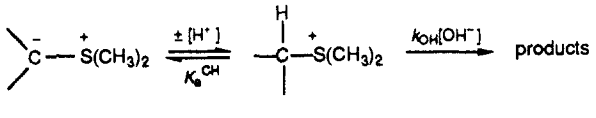
Second-order rate constants for base-catalyzed C(9) proton, deuteron, and triton exchange were obtained from the least-squares slopes of plots of k_{obsd} against the concentration of free base in the reaction mixture. When catalysis was determined at more than one value of pL, the second-order rate constants generally were found to agree within ±10%. Catalysis by acetate ion of ^1H and ^3H exchange from **1a** was determined at two or more values of pL and the errors in the second-order rate constants were obtained from the standard error of the least-squares slope for ≥8 values of k_{obsd}. For strongly basic catalysts, an external buffer with a pK_a that is below the pK_a of the catalyst was used to maintain a constant pL near the pK_a of the external buffer. First-order rate constants for catalysis by lyoxide ion were obtained from the intercepts of plots of k_{obsd} against the concentration of free buffer base. Second-order rate constants for catalysis by lyoxide ion were obtained from the slopes of plots of these intercepts against lyoxide ion concentration. First-order rate constants for catalysis by water were obtained in solutions of HCl or DCl.

Table I. pK_a Values and Brønsted β Coefficients for Proton Abstraction from Dimethyl(2-substituted-9-fluorenyl)sulfonium Tetrafluoroborates Catalyzed by Substituted Acetate Ions[a]

X	pK_a^{CH}	β	β_{corr}[b]
H	13.7 (13.8)[c]	0.98 (0.89)[d]	0.82
Br	12.4	0.91	0.76
NO_2	10.6	0.75	0.63

[a] In 95% D_2O–5% Me_2SO (v:v) at 28 °C and ionic strength 1.0 M (KCl); however, the pK_a values are in H_2O. [b] Corrected for the solvation effect according to $\beta_{corr} = \beta_{obs}/(1 - \beta_s)$, as described in the text. [c] From a fit of the dependence on pH of the rate of hydrolysis according to eq 4; see text. [d] For ^3H exchange.

Scheme I



Measurements of pK_a. (a) The pK_a^{BD} values of the amine catalysts in 95% D_2O–5% Me_2SO (v:v) at 1 M ionic strength were determined by extrapolating the pD of gravimetrically prepared buffer solutions containing the acid and base forms at a 1:1 ratio to zero buffer concentration. The pK_a^{BH} values of the carboxylate and alkoxide catalysts were determined by potentiometric titration[29] in 95% H_2O–5% Me_2SO (v:v) at 1 M ionic strength and values of pK_a^{BD} in D_2O were then estimated by using the equation proposed by Bell:[30] $\Delta pK_a = 0.017pK_a^{BH} + 0.44$; other similar equations[26] give results that are not significantly different. (b) The pK_a^{CH} values of the substrates were determined spectrophotometrically[29] with a Perkin-Elmer Lambda 4B spectrophotometer. Solutions of potassium hydroxide in 95% H_2O–5% Me_2SO (v:v) were prepared with boiled water that was cooled under a stream of argon. The absorbance at 258 nm for **1a** and **1b** or at 400 nm for **1c** was extrapolated to zero time because the substrates slowly hydrolyze in alkaline solution. The absorbance of the ylides of **1a** and **1b**, A_{C^-}, was obtained from the intercepts of plots of A_{258} against $[H^+](A_{258} - A_{CH})$, in which A_{CH} is the absorbance of the carbon acid.[29] A small correction for the change in the activity of hydroxide ion was applied for potassium hydroxide concentrations >0.8 M using an acidity function for the ionization of indoles in concentrated potassium hydroxide.[31] The pK_a of **1a** was also determined kinetically by monitoring the rate of its hydrolysis as a function of pH at 257 nm. The reactions were first-order for $>3t_{1/2}$ and endpoints were determined after $>10t_{1/2}$. Pseudo-first-order rate constants were obtained from the slopes of semilogarithmic plots of $A_t - A_\infty$ against time. Similar experiments with **1b** yielded complex biphasic kinetics as a function of pH and were not analyzed further.

Results

Determinations of pK_a. The pK_a^{CH} values for the ionization of dimethyl(2-substituted-9-fluorenyl)sulfonium tetrafluoroborates were determined spectrophotometrically at equilibrium, as described in the Experimental Section, and the results are summarized in Table I.

These compounds slowly undergo hydrolysis in alkaline solution.[32] Figure 1 shows that the dependence of the pseudo-first-order rate constants on the concentration of potassium hydroxide is nonlinear for the hydrolysis of **1a** because it is converted to the unreactive anion at high pH, as shown in Scheme I. This

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(30) Bell, R. P. *The Proton in Chemistry*, 1st ed.; Cornell University Press: Ithaca, NY, 1959.

(31) Yagil, G. *J. Phys. Chem.* **1967**, *71*, 1034–1044.

(32) The hydrolysis products were not characterized; they may be methanol and the 9-fluorenyl thioether.

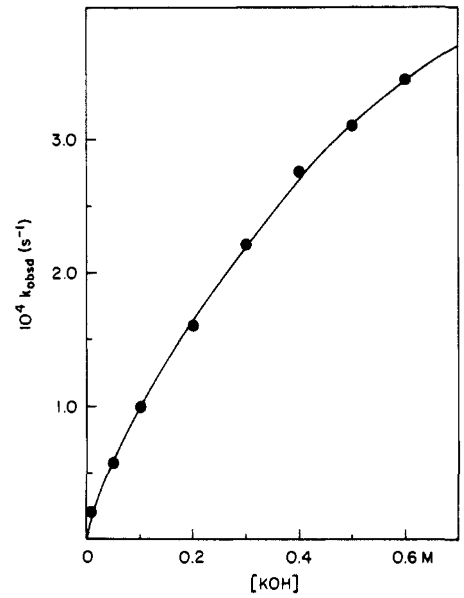

Figure 1. Dependence of the rate constant for hydrolysis of dimethyl-9-fluorenylsulfonium tetrafluoroborate (**1a**) on the concentration of hydroxide ion in 95% H_2O–5% Me_2SO (v:v) at 28 °C and ionic strength 1.0 M (KCl). The solid line is from a nonlinear least-squares fit of the data to eq 4 with $K_w = 1.05 \times 10^{-14}$, $k_{OH} = 1.1 \times 10^{-3}$ M^{-1} s^{-1}, and $K_{CH} = 1.5 \times 10^{-14}$ M ($pK_a^{CH} = 13.8$).

was used to determine the pK_a kinetically. A nonlinear least-squares fit of the data[33] to eq 4, which is derived from Scheme

$$k_{obsd} = K_w k_{OH}[OH^-]/K_a^{CH}([OH^-] + K_w/K_a^{CH}) \quad (4)$$

I, gave a second-order rate constant for hydrolysis of $k_{OH} = 1.1 \times 10^{-3}$ M^{-1} s^{-1} and $K_a^{CH} = 1.5 \times 10^{-14}$, or $pK_a^{CH} = 13.8$. This agrees with the spectrophotometrically determined value of $pK_a^{CH} = 13.7$. A value of $pK_a = 7.3$ for the bromide salt of **1a** in 31.7% water–dioxane has been reported.[34] Ingold and Jessop[24] have reported that the ylide **1a**$^\pm$ is not formed from the bromide salt of **1a** in aqueous sodium carbonate, which is consistent with $pK_a > 11$.

Kinetics. Pseudo-first-order rate constants for C(9)-^{1}H and ^{3}H exchange from dimethyl(2-substituted-9-fluorenyl)sulfonium ions **1a–c** were determined by ^{1}H NMR and detritiation in a series of amine and oxygen anion buffers in 95% D_2O–5% Me_2SO (v:v) at 28 °C and ionic strength 1.0 M (KCl), as described in the Experimental Section. The data were found to obey the rate law described by eq 5. Rates of exchange catalyzed by stronger bases

$$k_{obsd} = k_B[B] + k_{D_2O} + k_{OD}[OD^-] \quad (5)$$

were determined in the presence of a buffer with a low pK to maintain the pL constant, as illustrated in Figure 2 for ^{1}H and ^{3}H exchange from **1a** catalyzed by the anion of 1,1,1,3,3,3-hexafluoro-2-propanol. Catalysis by the relatively low concentration of free base was significant because of the large negative deviation of deuteroxide ion from the Brønsted correlations, which have slopes that approach 1.0 (see below). In a few cases total concentrations of the amine catalysts approaching 1 M were required in order to obtain a significant increase in rate. For buffers that showed no significant catalysis, an upper limit for the second-order rate constant was estimated by assuming that a 10% increase of the rate was caused by catalysis at the highest buffer concentration examined but was not detected.

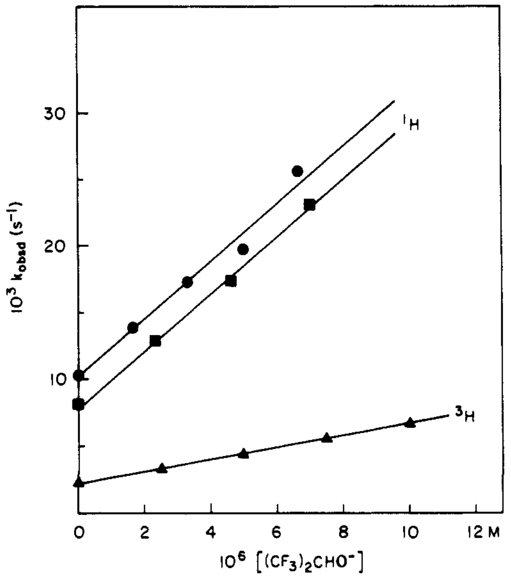

Figure 2. Dependence of the rate constants for C(9)-^{1}H (●,■) and ^{3}H (▲) exchange of dimethyl-9-fluorenylsulfonium tetrafluoroborate (**1a**) on the concentration of the anion of 1,1,1,3,3,3-hexafluoro-2-propanol in 95% D_2O–5% Me_2SO (v:v) at 28 °C and ionic strength 1.0 M (KCl). Buffers: ●, 0.03 M trifluoroethylamine, pD 6.02; ■, 0.05 M cyanomethylamine, pD 5.57; triangle, 0.0625 M acetate, pD 5.75.

Table II. Second-Order Rate Constants for General-Base Catalysis by Primary Amines of Proton Abstraction from Dimethyl(2-substituted-9-fluorenyl)sulfonium Tetrafluoroborates[a]

		k_B, M^{-1} s^{-1}	
catalyst	pK_a	**1a**	**1b**
$D_2NC(O)NDND_2$	4.36	2.1×10^{-3}	1.6×10^{-2}
CH_3OND_2	5.22	1.0×10^{-2}	6.4×10^{-2}
$NCCH_2ND_2$	6.10	6.3×10^{-2}	3.4×10^{-1}
$CF_3CH_2ND_2$	6.43	7.8×10^{-2}	5.5×10^{-1}
$CNCH_2CH_2ND_2$	8.64	5.4	2.1×10^{1}
$ClCH_2CH_2ND_2$	9.36	1.3×10^{1}	5.3×10^{1}
$DOCH_2CH_2ND_2$	10.45	6.5×10^{1}	2.7×10^{2}
$CH_3CH_2ND_2$	11.60	2.3×10^{2}	$<8.2 \times 10^{2}$

[a] In 95% D_2O–5% Me_2SO (v:v) at 28 °C, 1 M ionic strength (KCl); pK_a^{BD} values were determined as described in the Experimental Section.

The experimental results are summarized in Tables S1–S4 (see paragraph concerning supplementary material) and the second-order rate constants for catalysis by primary amines and oxygen catalysts are summarized in Tables II and III, respectively. Table III also contains data for ^{2}H exchange catalyzed by CH_3COO^- and ^{3}H exchange catalyzed by H_2O, CH_3COO^-, and OH^- in 95% H_2O–5% Me_2SO (v:v).

Specific salt effects are small. No significant change (<5%) of the second-order rate constant for acetate-catalyzed proton exchange of **1a** in D_2O was observed when potassium trifluoroacetate was substituted for potassium chloride (Table S1) in order to maintain constant ionic strength, and no catalysis was observed by CF_3COO^- itself at concentrations up to 1 M. For a given buffer ratio the observed pH varied by ≤0.04 pH unit for most catalyst concentrations examined and corrections were not made for these changes of pH. Control experments[35] using *p*-nitrophenolate anion as an indicator showed an increase in absorbance of ≤4% in 10 mM acetic acid buffers (pD 5.27) containing 0–1.0 M ethylamine deuterochloride and 4 mM *p*-nitrophenol. A decrease of 12% in the absorbance was predicted from the decrease of 0.12 pH unit in the apparent pH. These concentrations of buffer and catalyst are similar to those that were used to determine some of the rate constants for amine catalysis in Table II. Changes in pH with changes in buffer concentration may represent changes in the junction potential of the reference electrode.[35]

Primary kinetic isotope effects, k_L/k_T, for C(9)-hydron exchange and secondary solvent isotope effects, k_{H_2O}/k_{D_2O}, for triton

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(33) Computer programs for the nonlinear least-squares fit to the data were kindly provided by Dr. Niel Stahl. The minimization of the residual deviations was performed by a program similar to that described by Beech, G. *FORTRAN IV in Chemistry: An Introduction to Computer-Assisted Methods*; John Wiley: New York, 1975; pp 41–47.

(34) Johnson, A. W.; LaCount, R. B. *Tetrahedron* **1960**, *9*, 130–138.

(35) Stahl, N.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 4196–4205.

Table III. Second-Order Rate Constants for General-Base Catalysis by Oxygen Catalysts of Hydron Exchange from Dimethyl(2-substituted-9-fluorenyl)sulfonium Tetrafluoroborates **1**[a]

catalyst	pK_a[b]	C(9)-H	k_B, M^{-1} $^{-1}$ **1a**	**1b**	**1c**
D_2O	-1.74	^1H	$2.1 \times 10^{-6}/54.8$	$1.7 \times 10^{-5}/54.8$	$2.4 \times 10^{-4}/54.8$
		^3H	$9.7 \times 10^{-7}/54.8$		
H_2O[c]	-1.74	^3H	$2.2 \times 10^{-6}/54.8$		
CF_3COO^-	0.69	^1H	$<3.1 \times 10^{-7}$		
Cl_2CDCOO^-	1.68	^1H	5.6×10^{-6}	1.0×10^{-4}	5.2×10^{-3}
$NCCH_2COO^-$	2.74	^1H	7.3×10^{-5}	1.0×10^{-3}	2.7×10^{-2}
		^3H	2.6×10^{-5}		
$CH_3OCH_2COO^-$	3.88	^1H	8.8×10^{-4}	1.3×10^{-2}	1.7×10^{-1}
		^3H	2.6×10^{-4}		
CH_3COO^-	5.24	^1H	$(1.75 \pm 0.03) \times 10^{-2}$	1.7×10^{-1}	2.1
		^3H	$(4.24 \pm 0.17) \times 10^{-3}$		
	4.72[c]	^2H	$(8.06 \pm 0.13) \times 10^{-3}$		
		^3H	$(5.19 \pm 0.14) \times 10^{-3}$		
$(CF_3)_2CHO^-$	10.05	^1H	2.10×10^2	1.1×10^3	1.6×10^4
		^3H	4.5×10^1	1.9×10^2	
$CF_3CH_2O^-$	13.07	^1H	$<4.7 \times 10^1$		
DO^-	16.61[d]	^1H	5.9×10^4	3.3×10^5	3.7×10^6
		^3H	7.2×10^3	7.8×10^4	
HO^-	15.72[c,d]	^3H	3.9×10^3	3.7×10^4	

[a] In 95% D_2O–5% Me_2SO (v:v) at 28 °C, 1 M ionic strength (KCl) unless otherwise indicated. [b] Values of pK_a refer to D_2O unless otherwise indicated and were determined as described in the Experimental Section. [c] In 95% H_2O–5% Me_2SO (v:v). [d] Calculated from the concentration-based ionization constants of water in H_2O–Me_2SO mixtures reported by P. Fiordiponti, F. Rallo, F. Rodante (*Z. Phys. Chem.* **1974**, *88*, 149–159), assuming the same isotope effect on K_w as for pure water (Schowen, K. B., Schowen, R. L. *Adv. Enzymol.* **1982**, *87*, 551–606).

Table IV. Summary of Primary and Secondary Solvent Kinetic Isotope Effects[a]

base catalyst	carbon acid	ΔpK_a[b]	k_L/k_T[c]	k_{H_2O}/k_{D_2O}[d]
OD^-	**1b**	3.3	4.2	2.1
	1a	2.0	8.2	1.9
$(CF_3)_2CHO^-$	**1b**	-3.0	5.8	
	1a	-4.3	4.7	
CH_3COO^-	**1a**	-9.0	4.13 ± 0.18 1.55 ± 0.05[e]	1.22 ± 0.06
$CH_3OCH_2COO^-$	**1a**	-10.3	3.4	
$NCCH_2COO^-$	**1a**	-11.4	2.8	
D_2O	**1a**	-15.4	2.2	2.3

[a] Estimated errors are within ±10% unless otherwise indicated. [b] $\Delta pK_a = pK_a^{BH} - pK_a^{CH}$. [c] Primary kinetic isotope effect in 95% D_2O–5% Me_2SO (v:v); L = ^1H unless otherwise noted. [d] Secondary solvent isotope effect for triton exchange. [e] In H_2O with L = ^2H.

exchange were calculated from the second-order rate constants in Table III and are summarized in Table IV.

Discussion

Brønsted Correlations. Figure 3A shows that the rate constants for catalysis by primary amines of proton exchange from dimethyl(2-substituted-9-fluorenyl)sulfonium tetrafluoroborates (**1a–c**) in D_2O follow Brønsted correlations with slopes of β = 0.70 ± 0.01 and 0.75 ± 0.02 for **1a** and **1b**, respectively. The rate constants for catalysis by ethylamine show a small negative deviation and were not included in the correlation because one of them is an upper limit. The weakly basic "α-effect" compounds, semicarbazide and methoxyamine, do not show enhanced reactivity compared with other primary amines, in agreement with previous conclusions for proton transfer from carbon.[12a,36]

The increase in β from 0.70 to 0.75 with decreasing reactivity of the carbon acid is small but significant. This difference is demonstrated more clearly by the negative slope for the ratio of the rate constants for the two carbon acids in the Brønsted plot shown in Figure 3B; if the Brønsted slopes for **1a** and **1b** were the same, the slope of this correlation would be zero. The Brønsted plots in Figure 3A also appear to show downward curvature, as indicated by the dashed line, especially if the upper limit of the rate constant for ethylamine is included. However, such curvature is difficult to evaluate and we do not conclude at this time that the presence of curvature is definitely established.

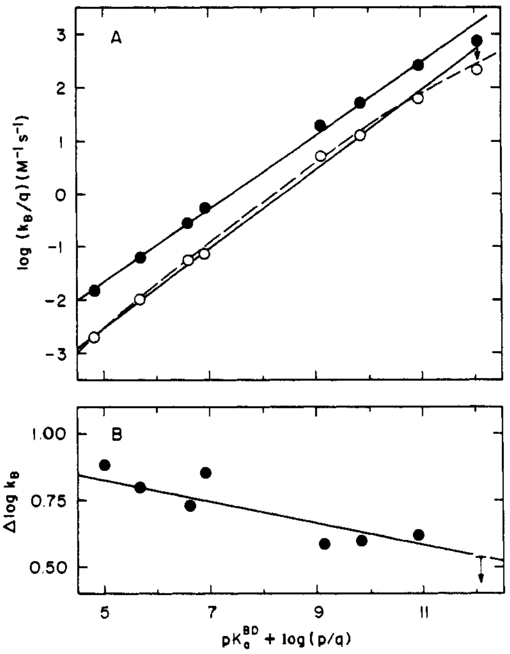

Figure 3. A. Statistically corrected Brønsted plots for base-catalyzed C(9)-^1H exchange from dimethyl-9-fluorenylsulfonium tetrafluoroborate (**1a**) (○) and dimethyl(2-bromo-9-fluorenyl)sulfonium tetrafluoroborate (**1b**) (●) by primary amines in 95% D_2O–5% Me_2SO (v:v). The rate constant for ^1H exchange from **1b** catalyzed by ethylamine represents an upper limit. The solid lines have slopes of β = 0.75 and 0.70. The dashed line was calculated from eq 7 with $p_y = \partial\beta/-\partial pK_a^{BD}$ = 0.04, as described in the text. B. The logarithm of the ratios of the rate constants, k_B, for C(9)-^1H exchange of **1a** and **1b** plotted against the pK_a of the amine catalyst.

Figure 4 shows Brønsted plots for catalysis of proton exchange by anionic oxygen catalysts and D_2O. The ordinate scale in Figure 4 is shifted by a factor of C = 1.3 for **1b** and 3.0 for **1c**, in order to facilitate comparison of the Brønsted curves for the three carbon acids. The slopes for catalysis by substituted carboxylate ions decrease from β = 0.98 for **1a** to 0.91 for **1b** and 0.75 for **1c**; the result for **1a** has been reported in a preliminary communication.[37]

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[36] Pratt, R. F.; Bruice, T. C. *J. Org. Chem.* **1972**, *37*, 3563-3567. Bruice, P. Y. *J. Am. Chem. Soc.* **1984**, *106*, 5959-5964.

[37] Murray, C. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1988**, *110*, 7561-7563.

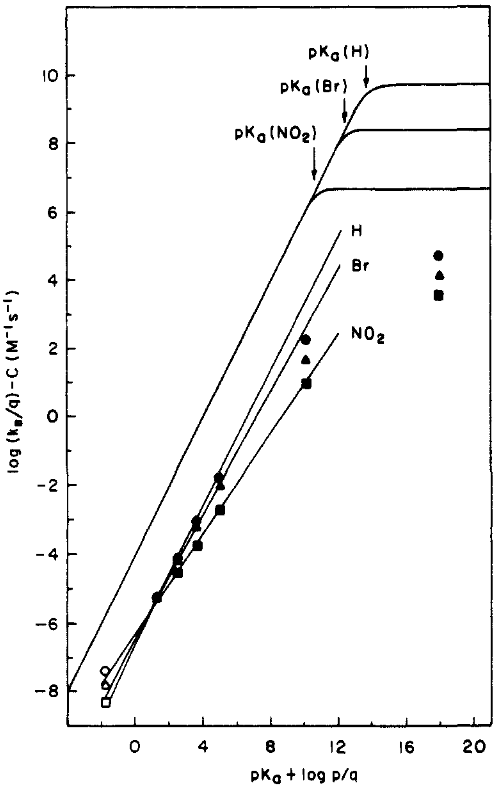


Figure 4. Normalized Brønsted plots for general base catalysis of C-(9)-^1H exchange catalyzed by oxygen bases from dimethyl-9-fluorenylsulfonium tetrafluoroborate (**1a**) (●), dimethyl(2-bromo-9-fluorenyl)sulfonium tetrafluoroborate (**1b**) (▲), and dimethyl(2-nitro-9-fluorenyl)sulfonium tetrafluoroborate (**1c**) (■) in 95% D_2O–5% Me_2SO (v:v). The open symbols refer to D_2O as a catalyst. The left ordinate scale is shifted by a factor $C = 1.3$ for **1b** and $C = 3.0$ for **1c**. The solid bold lines are theoretical Eigen curves for diffusion-controlled proton transfer, calculated from $k_B = K_a^{CH} k_{BH}/Ka^{BH}$ with $k_{BH} = 5 \times 10^9$ M^{-1} s^{-1} for thermodynamically unfavorable proton exchange and $k_B = 3 \times 10^9$ M^{-1} s^{-1} for thermodynamically favorable transfer. The light lines have slopes of $\beta = 0.98$ (**1a**), $\beta = 0.91$ (**1b**), and $\beta = 0.75$ (**1c**) through the points for the $RCOO^-$ catalysts.

These changes in the Brønsted β values occur over a range of reactivity of the carbon acids of ~100–1000-fold. The decrease in the ratio of the rate constants for **1c** and **1a** from 1000 with dichloroacetate to 76 for hexafluoroisopropoxide ion as the base is a consequence of the decrease in β for the more reactive carbon acid. There are large negative deviations of the rate constants for catalysis by deuteroxide ion, which is more basic than the ylide product, and a smaller deviation for hexafluoroisopropoxide ion.

The existence of a significant change in these Brønsted slopes with changing reactivity of the carbon acid and the base is shown more clearly by the Brønsted plots of rate constant ratios for different base catalysts with the three carbon acids in Figure 5. The changing slopes of the correlations show that there is a change in sensitivity to the acidity of the carbon acid with changing basicity of the catalyst. Table V shows the increase in the absolute values of α for the carbon acids with decreasing basicity of anionic oxygen catalysts. The absolute values of α are not as reliable as the values of β for the base catalysts, because of the small number of compounds examined and the possibility of perturbation of the α values because of resonance into the fluorene ring. However, there is no doubt about the *change* in α and the large values of α suggest that there is little, if any, decrease in the values from resonance.

The smaller values of α for water compared with anionic catalysts is consistent with an electrostatic interaction between the negative charge of the anions and substituents on the carbon acids. An electron-withdrawing substituent that increases the acidity of the carbon acid may interact favorably with the negative charge of the anion and stabilize the transition state.[3] This increases the rate constant for carbon acids of lower pK_a, compared with uncharged catalysts, and therefore increases α.

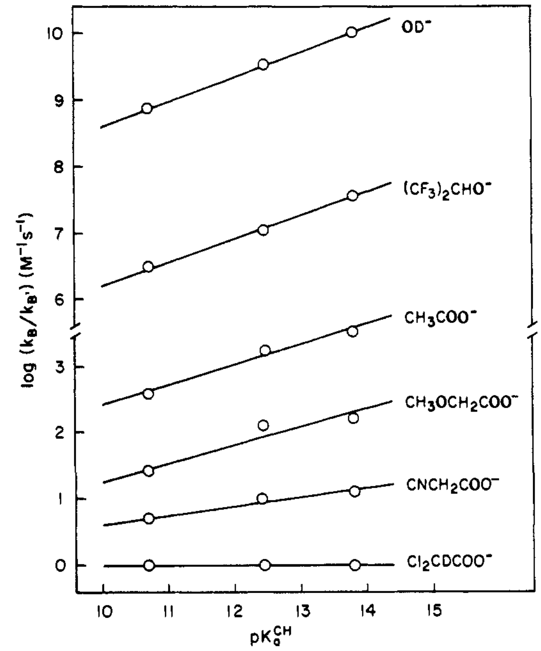


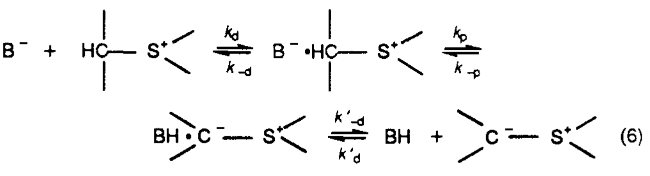
Figure 5. The change in the dependence of the rate constants, k_B, for C(9)-^1H exchange in D_2O catalyzed by $RCOO^-$ and RO^-, relative to the rate constant, k_B', for exchange catalyzed by $CDCl_2COO^-$, on the pK_a of the carbon acid in H_2O.

Table V. Brønsted α Coefficients for General-Base-Catalyzed Proton Abstraction from Dimethyl(2-substituted-9-fluorenyl)sulfonium Tetrafluoroborates[a]

catalyst	pK_a	α
OD^-	16.61	0.59
$(CF_3)_2CHO^-$	10.05	0.64
CH_3COO^-	5.24	0.68
$CH_3OCH_2COO^-$	3.88	0.74
$NCCH_2COO^-$	2.74	0.84
Cl_2CDCOO^-	1.68	0.97
D_2O	-1.74	0.68

[a] In 95% D_2O–5% Me_2SO (v:v) at 28 °C and ionic strength 1.0 M (KCl).

The large Brønsted slopes and the curvature of the Brønsted plots in Figure 4 might suggest a mechanism of diffusion-controlled proton transfer in the thermodynamically favored direction, as described by Eigen for normal acids[16] (eq 6). The Brønsted slopes of close to unity for acetate ions would then represent rate-limiting diffusional separation of RCOOH from the ylide after proton transfer (k'$_{-d}$, eq 6). However, this interpretation is excluded by the following:



(1) The primary kinetic isotope effects of k_H/k_T = 3–6 for hydron exchange catalyzed by general bases (Table IV) are inconsistent with rate-limiting diffusional separation of the conjugate acid from the ylide (k'_{-d}, eq 6). The isotope effects decrease with increasing ΔpK between the proton donor and acceptor, but there is still a significant isotope effect for proton abstraction by D_2O. This reaction represents protonation of the ylide by the hydronium ion in the reverse direction, which is thermodynamically favorable by 12–15 pK units.

(2) The bold lines in Figure 4 are calculated from the values of pK_a^{CH} that were determined spectrophotometrically and describes the limiting Eigen curves that are expected for diffusion-controlled reactions, according to eq 6.[38] The rate constants

Table VI. Summary of Cross-Interaction Coefficients, p_{xy}, for Proton Transfer to and from Carbon[a]

base	acid	$k_0{}^b$, M^{-1} s^{-1}	$p_{xy} = \partial\beta/\partial pK_a{}^{CH}$	reactivity range	ref
$RCOO^-$	dimethyl-9-fluorenylsulfonium tetrafluoroborates	10^5	0.07[c]	10^6	d
RND_2	dimethyl-9-fluorenylsulfonium tetrafluoroborates	10^4	0.04	10^5	d
RR′NH	(*p*-nitroaryl)acetonitriles	10^3	0.053	10^3	e
$RCOO^-$	mono- and dicarbonyl compounds	10^2	0.04	10^{10}	f
vinyl ethers	RCOOH		≤0.036[g]	10^6	h
RR′NH	1-aryl-1-nitroethanes	10^{-3}	~0	10^3	i

[a] In water at 25 °C unless otherwise indicated. [b] Rate constant at $\Delta pK = 0$ from interpolations or extrapolations of the Brønsted plot. [c] Calculated from the Brønsted β values corrected for solvation effects (Table I); see text. [d] This work, in 95% D_2O–5% Me_2SO (v:v) at 287 °C. [e] From a comparison of the *o*-nitro and unsubstituted compounds, in 50% Me_2SO–50% H_2O (v:v) at 28 °C; ref 9. The value of p_{xy} might be influenced by resonance with the *o*-nitro substituent. [f] Reference 30. The experimentally measured values for the pK_a of acetone (pK_a = 18.9; Tapuhi, E.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 5758–5765) and chloroacetone (pK_a = 15.8; Guthrie, R.; Cossar, J. *Can. J. Chem.* **1986**, *64*, 1250–1266) were used in the correlation. The Brønsted β values are 0.57 for acetylacetone ionization at 20 °C (ref 19) and 0.77 for vinyl alcohol ketonization at 15 °C (ref 51), which corresponds to base catalyzed enolization of acetaldehyde (pK_a = 16.7; Chiang, Y.; Hojatti, M.; Keeffe, J. R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000–4009) in the reverse direction, were used in the correlation. [g] This value is an upper limit because it was estimated from $p_{xy} = -\partial\alpha/\partial \log k$, instead of $\partial\alpha/\partial \log K$; k is the rate constant for protonation of a series of enol ethers by an acid of pK = 4.0 that was obtained from interpolation of the Brønsted plots. Values of K, the equilibrium constant for protonation of the enol ethers, are not available. [h] Reference 10. [i] Reference 12; a range of $p_{xy} = -0.022 \pm 0.022$ has been estimated for this coefficient (Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 4343).

corresponding to these lines are ≥100-fold larger than the observed rate constants for proton exchange in the thermodynamically unfavorable direction.

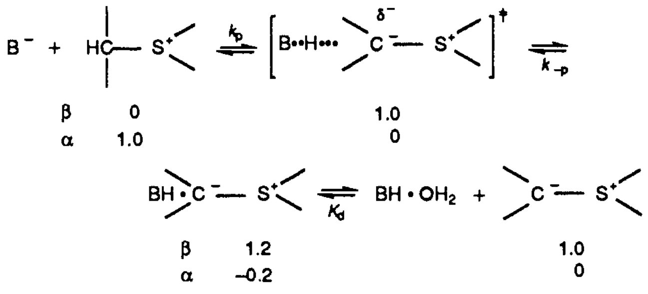
(3) The second-order rate constants of $k_{OD} = <10^4$ M^{-1} s^{-1} for the reactions of deuteroxide ion are at least 4 orders of magnitude smaller than expected for a diffusion-controlled reaction, although the reactions are thermodynamically favorable by 2–3 pK units.

(4) The rate constants of $k_0 \sim 10^4$ M^{-1} s^{-1} at $\Delta pK = 0$ for anionic oxygen bases, obtained from small extrapolations of the Brønsted plots, show that there is a significant intrinsic barrier for proton transfer. This value is much smaller than the values of $k_0 \sim 10^9$ M^{-1} s^{-1} for proton transfer to form carbanions that have little or no resonance stabilization and that are formed with diffusion-controlled separation of the products in the thermodynamically unfavorable direction.[39,40]

(5) The primary kinetic isotope effects of $k_H/k_T = 4.13 \pm 0.18$ (in D_2O) and $k_D/k_T = 1.55 \pm 0.05$ (in H_2O) for hydron exchange from **1a** catalyzed by acetate ion, are related by the Swain–Schaad[41] relation: $\ln(k_H/k_T)/\ln(k_D/k_T) = 3.24 \pm 0.25$. This value agrees with the theoretical[41] value of 3.26 and is consistent with a proton-transfer step that limits the overall rate of exchange. In particular, it shows no indication of significant internal return ($k_{-p} > k'_{-d}$ in eq 6), which is required for rate-limiting diffusional separation of products according to the Eigen mechanism.[42]

We conclude that the large Brønsted slopes shown in Figure 4 and Table I represent rate-limiting proton transfer, k_p in eq 6, with little or no contribution of the diffusional separation step. Large Brønsted β values and small primary kinetic isotope effects have been observed for thermodynamically unfavorable proton transfers from several other carbon acids that require relatively little electron delocalization and solvation upon ionization, such as acetylenic, halogen, cyano, and sulfonyl-activated acids.[43–45]

Scheme II



Solvation. The large Brønsted β values for catalysis of proton exchange from **1** by substituted actetate ions have been explained by a requirement for solvation of the conjugate acid of the catalyst by hydrogen bonding to water, $RCOOH{\cdot}OH_2$, as illustrated in Scheme II.[37] An observed value of $\beta = 1.0$ for proton removal in the transition state is the same as $\beta = 1.0$ for complete proton transfer at equilibrium, and both of these values correspond to $\alpha = 0$ for protonation by BH in the reverse direction. However, before protonation of the carbanion can occur, a solvating water molecule must first be removed from $BH{\cdot}OH_2$, with breaking of a hydrogen bond, and this is expected to be more difficult as the acidity of BH increases, with $\alpha \sim -0.2$.[46–49] Therefore, the α value of zero and the β value of 1.0 for catalysis represent a small but significant interaction of BH with the ylide in the transition state, which is approximately as strong as its interaction with water. This corresponds to $\beta_{corr} = \beta_{obs}/(1 - \beta_s) = 0.98/1.2 = 0.82$ and $\alpha = 0.18$ for protonation, in the reverse direction. The corrected values of β for **1a**, **1b**, and **1c** are shown in Table I.

In general, the requirement for desolvation of the carboxylic acid in the reverse direction means that the observed value of β for carboxylate ions overestimates the amount of bond formation in the transition state for reactions when β is large (and α is small). This is because the reference equilibrium reaction is the ionization of the *solvated* species $RCOOH{\cdot}OH_2$ to form the carboxylate anion $RCOO^-$.[50] The effect of solvation of the acid RCOOH

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(38) Theoretical Eigen curves were calculated as follows: for thermodynamically unfavorable proton transfer $k_B = K_a{}^{CH} k_{BH}/K_a{}^{BH}$ with $k_{BH} = 5 \times 10^9$ M^{-1} s^{-1} and for thermodynamically favorable proton transfer $k_B = 5 \times 10^9$ M^{-1} s^{-1}. Note that this definition assumes the $\Delta pK_a = pK_a{}^{BL} - pK_a{}^{CL}$ is the same in H_2O and in D_2O.

(39) Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 7117–7126.

(40) Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 674–683.

(41) Swain, C. G.; Stivers, E. C.; Reuwer, J. F., Jr.; Schaad, L. J. *J. Am. Chem. Soc.* **1958**, *80*, 5885–5893. The secondary solvent isotope effect for triton transfer ($k_{H_2O}/k_{D_2O} = 1.22$) is assumed to be the same for proton and deuteron transfer.

(42) An upper limit for the internal return ratio of $k_{-p}/k'_{-d} < 1/3$ for ^1H exchange (eq 6) was calculated from the extremes of the isotope effects and the Streitwieser modification of the Swain–Schaad relationship: Streitwieser, A., Jr.; Hollyhead, W. B.; Sonnichsen, G.; Pudjaatmaka, A. H.; Chang, C. J.; Kruger, T. L. *J. Am. Chem. Soc.* **1971**, *93*, 5096–5102. A value for the Swain–Schaad exponent of 3.26 was assumed and the equilibrium isotope effect $K_H/K_T = 1.2$ was estimated from the fractionation factors for sp³ (methine) C–H bonds.[26]

(43) Lin, A. C.; Chiang, Y.; Dahlberg, D. B.; Kresge, A. J. *J. Am. Chem. Soc.* **1983**, *105*, 5380–5386.

(44) Hibbert, F.; Long, F. A.; Walters, E. A. *J. Am. Chem. Soc.* **1971**, *93*, 2829–2835.

(45) (a) Bell, R. P.; Cox, B. G. *J. Chem. Soc. B* **1971**, 652–656. (b) Hibbert, F. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1289–1292.

(46) A value of $\alpha_d = -\beta_s = \partial \log K_d/\partial pK_a \approx -0.2$ for desolvation was estimated[37] on the basis of equilibrium constants for the interconversion of 1-arylethyl alcohols and ethers,[47] the data collected by Guthrie for replacement of the OH group by OCH_3 at carbon, phosphorus, and sulfur centers,[48] and the difference in free energy of transfer from the gas phase to water for a series of substituted phenols, compared with the corresponding benzenes,[49] that give values of $\alpha_d = -0.25$ for breaking a hydrogen bond from ROH to water.

(47) Rothenberg, M. E.; Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 1340–1346.

(48) Guthrie, J. P. *Can. J. Chem.* **1978**, *56*, 2342–2354.

(49) Hine, J.; Mookerjee, P. K. *J. Org. Chem.* **1975**, *40*, 292–298.

(defined by $\beta_s = -\partial \log K_d/\partial pK_a$) is to expand the scale for the Brønsted β coefficient from 1.0 to ~1.2, as outlined in Scheme II.[37,50] In order to obtain an estimate of the amount of bond formation to the base catalyst in the transition state for the k_p step, the observed value of β must be corrected for the solvation step.

Changes in Structure–Reactivity Coefficients. The negative slope of the correlation of rate constant ratios with increasing pK_a of amine catalysts in Figure 3B and the increasing values of α for the carbon acids with decreasing pK_a of the anionic catalysts shown in Figure 5 and Table V are consistent with an increase in the amount of proton transfer from the carbon acid in the transition state as the pK_a of the base catalyst is decreased. Changes in the amount of proton transfer to the base catalyst are also shown by the increase in the values of β for catalysis by substituted acetates with increasing pK_a of the carbon acid in Table I and Figure 4.

These changes are described by the interaction coefficient $p_{xy} = \partial\beta/\partial pK_a^{CH} = \partial\alpha/-\partial pK_a^{BH} = 0.04$ for amine catalysts (eq 2). The observed β values give a value of $p_{xy} = 0.08$ for anionic oxygen catalysts while the corrected β values (Table I) give $p_{xy} = 0.07$; these values do not differ significantly. A value of $p_{xy} = 0.08$ is also obtained from a plot of α (Table V) against pK_{BH} (not shown). The positive sign of these coefficients correspond to a normal "Hammond effect"; the Brønsted β value increases as the carbon acid becomes less reactive, and the sensitivity of the rate to the acidity of the carbon acid, α, increases with weaker bases. The sign of the p_{xy} coefficient is opposite to that expected for a direct electrostatic interaction between dipoles of the substituents on the carbon acids and base catalysts.[47]

Table VI summarizes data which suggest that the tendency of the transition state for proton transfer to undergo a change in structure, as measured by the p_{xy} coefficient, generally decreases as the intrinsic barrier increases. This is the behavior that is expected from an increase in the curvature of the energy surface at the transition state as the barrier increases. The increase in the intrinsic barrier corresponds to the decrease in k_0 for proton transfer at $\Delta pK = 0$ in Table VI. There is a linear increase in the Brønsted β values for proton transfer to substituted acetate ions from carbonyl-activated substrates with increasing pK_a of the carbon acid,[2,8,30] which has been confirmed and extended with rate constants for the ketonization of vinyl alcohol[51] and the ionization of acetylacetone.[19] Catalysis of the ionization of 1-aryl-1-nitroethanes by secondary amines, which has a large intrinsic barrier, shows no detectable change in β over a 1000-fold range of reactivity.[12]

Curvature of a Brønsted plot for base catalysis represents a decrease in slope with increasing pK_a of the catalyst and is described by a direct interaction coefficient, $p_y = \partial\beta/-\partial pK_a^{BH}$ (eq 1).[3] The Brønsted plots in Figure 3 for catalysis of the ionization of **1a** and **1b** by primary amines are consistent with a value of $p_y \sim 0.04$, and can be described satisfactorily by eq 7. The dashed

$$\log k = -\tfrac{1}{2}p_y(pK_a)^2 + \beta_0(pK_a) - F \qquad (7)$$

line in Figure 3A for **1a** was calculated from eq 7 with $p_y = 0.04$, $\beta_0 = 1.06$, and $F = 7.38$. However this estimate of p_y should be regarded as an upper limit because the presence of curvature is not certain. The results also illustrate that it is more difficult to demonstrate a significant direct coefficient that gives curvature than a cross coefficient that gives a change in the slopes of a series of Brønsted lines. The small value of p_y for these proton-transfer reactions with a modest intrinsic barrier suggests that carbon acids with larger barriers are unlikely to manifest significant curvature in Brønsted plots, in agreement with the conclusion of Bordwell and Hughes.[13]

The Nature of the Transition State. The Brønsted α and β values provide a measure of changes in charge distribution between the ground state and the transition state of proton-transfer reactions, which may provide a measure of the amount of proton transfer in the transition state. Changes in these parameters provide a measure of changes in charge distribution that may be related to measures of reaction progress and transition-state structure. Energy diagrams that are defined by the Brønsted values provide an empirical and self-consistent method for predicting and interpreting structure–reactivity parameters and changes in those parameters with changing structure of the reactants.[3]

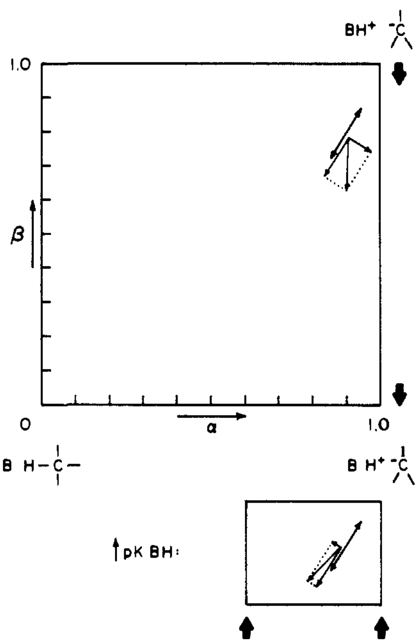

Figure 6. Energy contour diagram to describe the structure–reactivity behavior for proton transfer from dimethyl-9-fluorenylsulfonium ions to bases. The x and y axes are defined by the observed Brønsted coefficients α and β, respectively, and energy is a third dimension (contour lines not shown). The heavy arrows indicate a decrease in the energy of the right side of the diagram with decreasing pK_a of the carbon acid. The resulting change in the position of the transition state is indicated by the vertical arrow, which is the resultant of movements parallel and perpendicular to the reaction coordinate. The dashed lines indicate the observed range of structure–reactivity coefficients. The lower diagram shows the change in position of the transition state with increasing basicity of the base catalyst, which increases the energy at the bottom of the diagram. Reactions in which $\alpha \neq \beta$ show imbalance, which may arise from electron delocalization into the fluorenyl ring system that perturbs the observed value of α (see text), these changes do not necessarily reflect a change in bond order to carbon in the transition state.

The changes in the Brønsted α and β values that are defined by the coefficients p_x, p_y, and p_{xy} can be described by a reaction coordinate at a saddle point on the energy diagram of Figure 6, in which the x coordinate represents values of α for proton dissociation from carbon and the y coordinate represents values of β for proton transfer to the base catalyst; the contour lines for the energy are omitted. Movements of the transition state on the diagram are determined by the orientation of the reaction coordinate and by the curvatures a and b parallel to the x and y axis, respectively, and the diagonal curvature c. The curvatures calculated[3] from $p_x = 0$, $p_y = 0.04$, and $p_{xy} = 0.04$ are $a = 13$, $b = 0$, and $c = -25$. These curvatures correspond to "level lines" of constant energy through the saddle point at angles of 0° and 63° from the y axis.

The rectangle that is enclosed by dashed lines in Figure 6 indicates the range of the observed α and β values for the deprotonation of **1a–c**, and the center of the double headed arrow, which is rotated 63/2 = 32° from the y axis, describes the position of a transition state with $\alpha = 0.9$ and $\beta = 0.8$.

A decrease in the pK_a of the carbon acid corresponds to stabilization of the ylide and a decrease in the energy of the right side of the diagram, as indicated by the short, heavy arrows. This decrease in energy causes movement of the transition state toward

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[50] The changes in the solvation of $RCOO^-$ anions with pK_a are assumed to be negligible, as discussed in ref 18c. Note also that the requirement for (de)solvation follows from the fact that proton transfer to and from carbon is direct (Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 7126–7134).

[51] Capon, B.; Zucco, C. *J. Am. Chem. Soc.* **1982**, *104*, 7567–7572.

the position of lower energy in the direction *perpendicular* to the reaction coordinate and toward the position of higher energy in the direction *parallel* to the reaction coordinate, as indicated by the small arrows. The amounts of movement are determined by the direction of the reaction coordinate and the curvatures of the surface, *a*, *b*, and *c*. The net movement that is calculated from *a*, *b*, and *c* in this case is downward, to decrease β (p_{xy} = 0.04), with no change in α (p_x = 0; this result is required by b = 0).[3]

An increase in the basicity of B^- corresponds to an increase in the energy of the bottom relative to the top of the diagram, as indicated by the heavy arrows below the inset under the large diagram. This causes the indicated movements perpendicular and parallel to the reaction coordinate, with a calculated net movement downward and to the left. This corresponds to a decrease in α (p_{xy} = 0.04) and a decrease in β (p_y = 0.04).

Although there appears to be downward curvature corresponding to a positive p_y coefficient in the Brønsted plots for catalysis by amines and anionic oxygen catalysts (Figures 3 and 5), this curvature is not definitely established for the amines and its magnitude is uncertain. If the p_y coefficient were zero, the level lines of constant energy through the saddle point would be parallel to the x and y axes, the reaction coordinate would be diagonal, and movements of the transition state parallel and perpendicular to the reaction coordinate would cancel so that there would be no movement toward or away from the perturbation; i.e. the p_x and p_y coefficients would be zero.[3]

This treatment provides an empirical characterization of the transition state in terms of experimental structure–reactivity parameters, with few if any assumptions. To the extent that these structure–reactivity parameters provide measures of the structure of the transition state, the energy diagram provides a characterization of the transition state.[3]

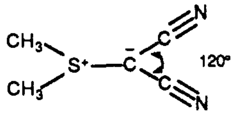
Changes in transition-state structure are comparatively easy to detect for the reactions of **1a–c** because of the relatively small intrinsic barrier and curvatures of the energy surface at the transition state for these reactions.[3,4,7,17] Still larger changes in transition-state structure are observed for the dissociation of thiazolium ions, which have a smaller intrinsic barrier and a small diagonal curvature of $c \approx -3.3$.[40] The changes in transition-state structure are expected to become larger as acids become more "normal", but they are difficult to detect for normal acids because diffusional steps become rate limiting for reactions with most bases.[16,17]

The dissociation of carbon acids shows *imbalance* when $\alpha \neq \beta$, which corresonds to a transition state that is not on the diagonal line between reactants and products in Figure 6. A positive p_{xy} coefficient will cause imbalance when the structure of the reactants is changed unless the p_x and p_y coefficients are large enough to prevent imbalance; it will always give rise to imbalance if p_x or p_y equals zero. The values of α and β shown in Tables I and IV show that there is a modest amount of imbalance in the reactions of **1a–c**. Imbalance tends to increase with increasing magnitude of the intrinsic barrier for proton transfer from carbon.[52] The intrinsic barrier in these reactions may be attributed largely to electron delocalization into the fluorenyl ring system, as discussed below, which is likely to perturb the observed values of α, compared with β, and give rise to the observed imbalance.

The Reactivity of Sulfonium Ions as Carbon Acids. The activating effect of the dimethylsulfonium group on the intrinsic reactivity of 9-fluorenyl carbon acids is very similar to that of the cyano group. The intrinsic barriers correspond to rate constants at $\Delta pK_a = 0$ of $k_0 \sim 10^4$ M^{-1} s^{-1} for dimethyl-9-fluorenylsulfonium ion and $k_0 = 10^{3.6}$ M^{-1} s^{-1} for 9-cyanofluorene in 90% H_2O–10% Me_2SO,[53] with primary amines as the proton acceptor. The values of k_0 for **1** were obtained from small extrapolations of the Brønsted plots in Figures 3A and 4.[54]

Most of the intrinsic barrier for these compounds can be attributed to delocalization into the fluorene ring, because the barrier for ionization of cyanocarbon acids is small: the intrinsic rate constant for proton transfer from bromomalononitrile to secondary amines is $k_0 = 10^7$ M^{-1} s^{-1}.[55] We conclude that the intrinsic barrier for the deprotonation of sulfonium ions is also small.

The activating effect of an α-sulfonium ion for the ionization of a carbon acid is much larger than that of an ammonium ion,[56] in spite of the larger C–S bond length of 1.82 Å compared with 1.50 Å for the C–N bond. The sulfonium ylide is presumably stabilized by the large polarizability of sulfur and may be stabilized by backbonding from carbon to d orbitals of sulfur by resonance, but there is still no consensus as to the importance of this resonance contribution.[57] The length of the C–S bond of the ylide **2**[58] is



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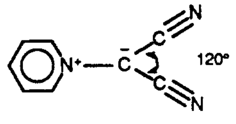

3

decreased by 0.10 Å compared with the C–S bond length of sulfonium salts[59] and there is a similar decrease of 0.08 Å in the C–N bond length of **3** compared with the C–N bond lengths of *N*-methylpyridinium ions, which may be attributed to the $N^+–C^-$ dipole.[60,61] The small intrinsic barrier that is contributed by the sulfonium group indicates that this much bond shortening does not provide a large contribution to an intrinsic barrier.

The small barrier for the formation of a sulfonium ylide indicates that most of the intrinsic barrier for the ionization of **1** arises from the structural reorganization that accompanies delocalization of negative charge into the fluorenyl ring system. The large dipole moment of μ = 6.3 D for **1a**$^\pm$, compared with μ = 4.9 D for trimethylamine *N*-oxide, shows that there is a large degree of charge separation in the ylide **1a**$^\pm$ that is consistent with an important contribution of resonance to the barrier.[62] These results also suggest that resonance delocalization in the absence of significant solvation of the activating group can give rise to modest barriers to proton transfer from carbon. This conclusion confirms and extends several previous observations.[15,53,63] For example, the detritiation of cyclopentadiene by methoxide ion in methanol is close to thermoneutral, but has a second-order rate constant of only 0.1 M^{-1} s^{-1}.[15]

Lyoxide Ion and Water-Catalyzed Exchange. The secondary lyoxide ion isotope effects of k^T_{OD}/k^T_{OH} = 1.9–2.1 for ^3H exchange of **1a** and **1b** in the thermodynamically favorable direction correspond to β = 0.8, according to the relationship $k^T_{OD}/k^T_{OH} = (2.4)^{\beta}$.[64] This agrees well with the corrected values of β = 0.82 and 0.76 for catalysis by acetate ions (Table I), although the rate

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[52] (a) Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335–2348. (b) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219–3234. (c) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301–308.

[53] Bernasconi, C. F.; Terrier, F. *Can. J. Chem.* **1986**, *64*, 1273–1275. Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1987**, *109*, 7115–7126.

[54] A value for $k_0 = 10^{3.4}$ M^{-1} s^{-1} can also be estimated from eq 7.

[55] Hibbert, F.; Long, F. A. *J. Am. Chem. Soc.* **1972**, *94*, 2647–2651.

[56] von E. Doering, W.; Hoffmann, A. K. *J. Am. Chem. Soc.* **1955**, *77*, 521–526.

[57] Mitchell, D. J.; Wolfe, S.; Schlegel, H. B. *Can. J. Chem.* **1981**, *59*, 3280–3292. Wolfe, S.; Stolow, A.; LaJohn, L. *Tetrahedron Lett.* **1983**, *24*, 4071–4074. Dixon, D. A.; Dunning, T. H., Jr.; Eades, R. A.; Gassmann, P. G. *J. Am. Chem. Soc.* **1983**, *105*, 7011–7017 and references cited therein.

[58] Christensen, A. T.; Witmore, W. G. *Acta Crystallogr., Sect. B* **1969**, *B25*, 73–78.

[59] Typical $S^+–CH_3$ bond lengths for methylsulfonium ions are 1.83 Å in trimethylsulfonium iodide (Zuccaro, D. E.; McCullough, J. D. *Z. Kristallogr.* **1959**, *112*, 401–408) and 1.82 Å in dimethylphenylsulfonium perchlorate (Lopez-Castro, A.; Truter, M. R. *Acta Crystallogr.* **1964**, *17*, 465–471).

[60] Bugg, C.; Sass, R. L. *Acta Crystallogr.* **1965**, *18*, 591–594.

[61] Typical $N^+–CH_3$ bond lengths for *N*-methylpyridinium ions are 1.49–1.50 Å: Carlström, D. *Acta Chem. Scand.* **1966**, *20*, 1240–1246. Leipoldt, J. G.; Basson, S. S.; Bok, L. D. C. *Acta Crystallogr., Sect. B* **1970**, *B26*, 361–367.

[62] Phillips, G. M.; Hunter, J. S.; Sutton, L. E. *J. Chem. Soc.* **1945**, 146–162.

[63] Okuyama, T.; Ikenouchi, Y.; Fueno, T. *J. Am. Chem. Soc.* **1978**, *100*, 6162–6166.

[64] Kresge, A. J. *Pure Appl. Chem.* **1964**, *8*, 243–258. Gold, V.; Grist, S. *J. Chem. Soc., Perkin Trans. 2* **1972**, 89–95. Kresge, A. J.; More O'Ferrall, R. A.; Powell, M. F. In *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol. 7, pp 177–273.

constants for catalysis by lyoxide ion fall well below a linear extrapolation of the Brønsted plots in Figure 4. It is possible that these rate constants reflect the well-known lyoxide ion anomaly, which may involve a requirement for partial desolvation of the lyoxide ion.[65] The difference between these values of β and the value of $\alpha = 0.59$ for **1a–c** represents imbalance, as noted above.

The secondary solvent isotope effect of $k_{H_2O}/k_{D_2O} = 2.3 \pm 0.2$ for ^3H transfer from **1a** to water (Table IV) shows that the initial kinetic unit that is formed upon proton exchange is HOL_2^+ and, therefore, that proton transfer to water is direct. This isotope effect agrees with the value of $k_{H_2O}/k_{D_2O} = 1/l^2 = 2.1$, calculated from the fractionation factor of $l = 0.69$ for HOL_2, but is smaller than $1/l^3 = 3.0$ for L_3O^+.[64] Furthermore, the absence of strong inhibition of ^1H and ^3H exchange by D_3O^+ (Table S4) shows that the reaction does not involve initial proton transfer through water to form a hydrogen-bonded species $>C^-\cdot{}^3HOH$ and H_3O^+ according to the Swain–Grunwald mechanism for hydron exchange.[66] Exchange by this mechanism is inhibited in the presence of acid because of reversal of the initial dissociation step, with return of the hydron to carbon before dissociation of $[^3H]H_2O$ into the bulk solvent.

Registry No. **1a**, 116724-74-4; **1b**, 124992-84-3; **1c**, 124992-86-5; Me_2S, 75-18-3; 9-bromofluorene, 1940-57-4.

Supplementary Material Available: Tables S1–S3 summarizing rate constants for general-base catalysis for hydron exchange from **1a–c** and Table S4 showing rate constants in aqueous LCl solutions for hydron exchange (5 pages). Ordering information is given on any current masthead page.

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(65) Hupe, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451–464. Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 683–692 and references therein.

(66) Emerson, M. T.; Grunwald, E.; Kaplan, M. L.; Kromhout, R. A. *J. Am. Chem. Soc.* **1960**, *82*, 6307–6314. Grunwald, E.; Ralph, E. K. *Acc. Chem. Res.* **1971**, *4*, 107–113. The small decrease in rate observed in 1 M HCl or DCl (Table S4) was also observed with HCN[39] and may be accounted for by an acidity function effect (Paul, M. A.; Long, F. A. *Chem. Rev.* **1957**, *57*, 1–45).

The Marcus Theory of Reactions of Quinolinium Ions with BH_4^- and OH^- [1]

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Abstract: The reactions of quinolinium ions with alkaline solutions of BH_4^- in a 4:1 mixture of 2-propanol and water were studied. Four 1-benzyl-3-cyanoquinolium ions and two 3-(aminocarbonyl)-1-benzylquinolinium ions were used. The quinolinium ions first reversibly add a nucleophile (mostly to the 4-position) and then are more slowly reduced to the 1,2- and 1,4-dihydroquinolines. The equilibrium constant for the addition of OH^- or OR^-, the rate constant for the addition, the rate constant for solvolysis of the adduct, and the rate constant for reaction of BH_4^- with the quinolinium ion were determined in each case. The quinolinium ion concentration was kept low enough so that only one of the hydridic hydrogens of BH_4^- was transferred to a quinolinium ion. Adduct formation and reduction by BH_4^- both have rates in the range 10^5–10^7 M^{-1} s^{-1}, and the Brønsted α values are similar. Both sets of rate constants can, roughly, be fitted by the Marcus theory of atom and group transfer if the intrinsic barrier is assumed to arise exclusively from the reorganization of the quinolinium ion. Since the presumptive critical complex for H^- transfer between BH_3 units, $B_2H_7^-$, is a known, stable ion, it is reasonable that the reorganization of BH_4^- does not contribute significantly to the intrinsic barrier for its reactions. The Marcus theory, and related ideas, such as the Leffler–Hammond principle, apparently can be usefully applied to reactions quite different from the original model, but the exact values of the derived parameters quite possibly do not have their apparent physical significance.

The dynamics of the reactions of quinolinium salts with tetrahydridoborate ion, BH_4^-, are of interest for a number of reasons. The major product of the reduction of quinolinium ions with a cyano or an aminocarbonyl group in the 3-position is the 1,2-dihydroquinoline, although, at equilibrium, about 95% of the products have the 1,4-structure.[2] An analogous discrepancy is also found in the reduction of pyridinium ions,[2] including the important enzymatic cofactor, nicotinamide adenine dinucleotide (NAD^+).[3] The formation of the 1,2-adduct precludes the use of BH_4^- as the ultimate reductant in the synthetic application of NADH-dependent enzymes.[4] The Marcus theory of atom and group transfer[5,6] provides another reason for interest. The theory contains the fundamental assumption that the potential energy surface leading from the precursor configuration to the critical configuration[7] is similar to that leading from the successor configuration to the critical configuration.[8] The formalism of the theory successfully describes a number of proton transfer rate constants, in which the structure and charge type of the reactants and products are different.[9,10] However, the intrinsic barriers, which are obtained by fitting the rate constants, sometimes differ considerably from expectations.[9,10] The present reactions are

Scheme I

$$1(OH) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 1^+ + OH^- \qquad (a)$$

$$1^+ + BH_4^- \longrightarrow \begin{cases} 1H \cdot BH_3 \\ 1H' \cdot BH_3 \end{cases} \qquad (b)$$

$$1H \cdot BH_3 + 3H_2O + OH^- \xrightarrow{\text{fast}} 1H + B(OH)_4^- + 3H_2 \qquad (c)$$

$$1H' \cdot BH_3 + 3H_2O + OH^- \xrightarrow{\text{fast}} 1H' + B(OH)_4^- + 3H_2 \qquad (d)$$

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(3) Werner, D. A.; Huang, C. C.; Aminoff, D. *Anal. Biochem.* **1973**, *54*, 554.

(4) (a) Whitesides, G. M.; Wang, C.-H. *Aldrichimica Acta* **1983**, *16*, 27. (b) Simon, H.; Gunter, H.; Bader, J.; Neuman, S. In *Enzymes in Organic Synthesis*; Ciba Foundation Symposium III, Pitman, London, 1985; p 97.

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